Remarks

Claims 10-11, 16, 39, 41 and 89-91 were pending in the instant application. Claims 39 and 41 have been withdrawn; claims 10 and 16 have been amended; and new claims 92-95 have been added. Support for these amendments and newly added claims can be found throughout the specification and the claims as originally filed, for example, at least in paragraphs [0010], [0014], [0023], [0131] and in the Examples starting at paragraph [0192].

In addition, the specification has been amended to include amino acid and nucleotide sequences and sequence identifiers for the Pin1 protein and Pin1 nucleic acid, respectively. Support for the amendment to the specification can be found at least at paragraph [0131 of the specification as originally filed, wherein U.S. Patents 5,952,647 and 5,972,697 were expressly incorporated into the present application by reference. *Accordingly, no new matter has been added.*

Upon entry of the amendment, claims 10, 11, 16, 39, 41 and 89-95 will be pending in the instant application. Amendments to and/or cancellation of claims should in no way be construed as an acquiescence to any of the Examiner's objections and/or rejections. The amendments to and/or cancellation of claims are being made solely to expedite prosecution of the above-identified application. Applicants reserve the option to further prosecute the same or similar claims in the present or another patent application. The amendments made to the claims are not related to any issues of patentability.

Sequence Listing

In view of the foregoing amendment to the specification and claims to include sequence identifiers, Applicant is filing concurrently herewith a copy of a Sequence Listing in computer readable form (CRF) and a paper copy, an amendment directing entry of the sequence listing in the specification, a statement that the content of the paper and CFR copies are the same and include no new matter as required by 37 CFR § 1.821 (b), (e), (f) or (g) or 1.825 (d). *No new matter has been added by the foregoing amendments.*

Claim Rejections Under 35 USC §112, 2nd Paragraph

Claims 10, 11, 16 and 89-91 were rejected as being indefinite on the ground that the use of the term "Pin1" renders the claim unclear because different laboratories may use the same laboratory designations to define completely distinct molecules.

Applicants traverse this rejection. Throughout the specification the term "Pin1 protein" is consistently referred to as a sequence and phosphorylation specific peptidyl-prolyl isomerase which catalyzes the isomerization of pSer/Thr-Pro bonds. Further, a number of scientific publications and patents are also recited which set forth the unique structural and functional characteristics of the Pin1 protein. Accordingly, the meaning of this term would be clear to the average artisan. However, solely in the interest of expediting prosecution, Applicants have amended the claims as suggested by the Examiner to include sequence identifies for the amino acid sequence of the Pin1 protein, thus rendering this rejection moot.

Claim Rejections Under 35 USC §112, 1st Paragraph

Claims 10, 11, 16 and 89-91 were also rejected as failing to comply with the written description requirement on the ground that the term Pin1 allegedly encompasses more than the full length protein of Pin 1, but also Pin 1 variants and homologs.

Applicants traverse this rejection at least for the reasons set forth above. However, solely in the interest of expediting prosecution, Applicants have amended the claims as suggested by the Examiner to include sequence identifies for the amino acid sequence of the Pin1 protein, thus rendering this rejection moot.

Claim Rejections Under 35 USC §103

Claims 10, 11, 16 and 91 were rejected as being unpatentable over any one of WO 97/17986, US Patent 5,972,697 or US Patent 5,952,467 on the ground that

> It would have been *prima facie* obvious to one of ordinary skill to one of ordinary skill in the art at the time the invention was made to use Pin1 detection as a means to gauge hyperproliferative disorders [as] well as detecting malignant growth. One of skill in the art would have been motivated in doing so because any one of WO 97/17986, US Patent 5,972,697 or US Patent 5,952,467 taught that Pin1 can be detected in tissue sample or bodily fluids using a Pin1 specific antibody and comparing the expression levels assessed

> from the experimental sample to normal controls. Although none of the references relied upon specifically teach that a higher standard deviation is to be indicative of malignancy, it would have been within the realm of standard experimentation and optimization for one of skill in the art. (Office Action pages 8-9)

Applicants traverse this rejection. Applicants note that WO 97/17986, US Patent 5,972,697 and US Patent 5,952,467 (hereinafter collectively referred to as "Hunter *et al.*"), generally disclose the concept of diagnosing cell proliferative disorders by detecting Pin1 levels. However, Hunter *et al.* do not appear to contain a specific disclosure of using *elevated* Pin1 levels as a specific marker of *malignant* cancer. Specifically, Hunter *et al.* teach that elevated Pin1 levels might be expected to be present in a number of cell proliferative disorders but does not distinguish between malignant disorders and non-malignant disorders such as benign cancers, psoriasis, pemphigus vulgaris, Bechet's syndrome, acute respiratory distress syndrome (ARDS), ischemic heart disease, post-dialysis syndrome, rheumatoid arthritis, acquired immune deficiency syndrome, vasculitis, lipid histiocytosis, septic shock and inflammation in general. Nor do Hunter *et al.* teach or suggest that there is any correlation between Pin1 levels and the aggressiveness of a cell proliferative disorder.

In contrast, the subject matter of the present claims is based on the discovery that Pin1 levels increase as cancer cells become more aggressive, *i.e.*, malignant (*e.g.*, see paragraph [0028] and Example 1). For example, the data presented in Figures 1 and 2 clearly demonstrate that the Pin1 level in the majority of the malignant breast cancer samples tested was higher than the mean plus three times standard deviation of the level found in the normal samples. Additionally, the data in Figures 1 and 2 further show that the average level of Pin1 in Stage II cancer samples (0.924) is higher than the mean plus 7.5 standard deviations of the level found in the normal samples [0.114 + (7.5 x .106) = 0.909], and that the average level of Pin1 in Stage III cancer samples (1.399) is higher than the mean plus 12 standard deviations of the level found in the normal samples [0.114 + (12 x .106 = 1.386]. Clearly, the specification does provide quantitative evidence that levels of Pin1 correlate with cancer stage, *i.e,* aggressiveness.

In short, the specific, quantitative measurement for distinguishing malignant from non-malignant cell proliferative conditions provided by the present invention would not have been *prima facie* obvious in view of the general disclosure of Hunter *et al.* and, accordingly, withdrawal of this rejection is respectfully requested.

Conclusion

It is respectfully submitted that this application is in condition for allowance. If a telephone conversation with Applicants' attorney would help expedite the prosecution of the above-identified application, the Examiner is urged to call the undersigned attorney at (617) 227-7400.

Dated: March 20, 2007

Respectfully submitted,

By _____

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